Remarks

Claims 22-31 were pending in the subject application. By this Amendment, the applicants have amended claim 27 and cancelled claims 22-26, 28 and 31. Support for the amendments to the claims can be found throughout the specification and claims as originally filed. No new matter has been added by these amendments. Accordingly, claims 27, 29 and 30 are before the Examiner for consideration.

The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. The amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 22-31 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The applicants respectfully traverse this ground for rejection to the extent that it might be applied to the claims as amended herein.

Claims 22-26 have been cancelled herein, thereby rendering moot this ground for rejection as it relates to those claims.

Claim 27 has been amended to address the issue raised by the Examiner with regard to antecedent basis for the term "presence or absence." Claim 27 has also been amended to lend further clarity to the claimed subject matter by removing reference to physical and chemical properties.

Additionally, claim 31 has been cancelled.

The test for definiteness under 35 U.S.C. §112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). The skilled artisan would have no difficulty ascertaining the metes and bounds of the claims now presented for examination. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Claims 22-31 have been rejected under 35 U.S.C. §102(b) as being anticipated by Douillard *et al.* (Meth. Enz. 92:168, 1983). The applicants respectfully traverse this ground for rejection because the Douillard *et al.* reference does not disclose each and every step of the applicants' advantageous multi-analyte assay wherein a negative control value is generated using capture reagents that have antigenic properties in common.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

Douillard *et al.* use, as negative control, irrelevant antigens while the assay of the subject invention uses antigenically related capture reagents. As set forth in the applicants' claims that are now presented for examination, the capture reagents that are used to generate the negative control value have antigenic properties in common with the capture reagents that detect the analytes of interest. Advantageously, this method creates a sample-specific negative control value that enhances the ability of this assay to accurately detect the presence or absence of analytes. For example, in the case of assaying for HLA antibodies, a variety of different HLA antigens can be used. Potentially any one of these antigens could react with antibodies in the sample. However, in all likelihood, an individual will not make antibody against self antigens, therefore, one or more antigens will be negative thereby providing the negative control value.

Douillard *et al.* do not disclose or suggest an assay utilizing an antigenically-related capture reagent that is used to determine the negative control value. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Douillard *et al.* reference.

Claims 22-31 have been rejected under 35 U.S.C. §102(b) as being anticipated by Hoffman *et al.* (U.S. Patent No. 5,599,543). The applicants respectfully traverse this ground for rejection because the Hoffman *et al.* reference does not disclose each and every step of the claimed assay wherein a negative control value is generated using capture reagents that are related to the capture reagents that are used to detect the analytes of interest.

The present invention requires the use of antigenically related capture reagents. With regard to Hoffman *et al.*, the Examiner notes the use of irrelevant antigens as negative controls within an immunological assay. Thus the ELISAs of Hoffman *et al.* fail to account for non-specific interaction of sample analytes and the "irrelevant" antigens used in the assay. The applicants' selection of a least reactive antigen as the sample-specific negative control resolves the non-specificity dilemma encountered by the use of "irrelevant" antigens. Importantly, the least reacting antigen will vary depending on the sample being tested.

Because Hoffman *et al.* do not disclose or suggest an assay having the steps as set forth in the current applicants' claims, those claims cannot be said to be anticipated. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Hoffman *et al.* reference.

Claims 22-31 have been rejected under 35 U.S.C. §102(b) as being anticipated by Geysen *et al.* (*Proc. Natl. Acad. Sci. USA* 81:3998-4002, 1984). The applicants respectfully traverse this ground for rejection because the Geysen *et al.* reference does not disclose each and every step of the claimed assay.

Geysen *et al.* do not disclose the use of an antigenically related capture reagent as a negative control. Once again, the applicants' selection of a sample-specific negative control differentiates the invention from the ELISA methods disclosed by Geysen *et al.* and others.

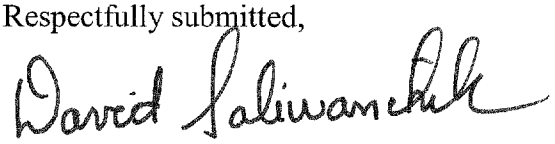
Geysen *et al.* do not disclose or suggest an assay utilizing an antigenically-related capture reagent that is used to determine the negative control value. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Geysen *et al.* reference.

In view of the foregoing remarks and the amendment above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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